

Amendments to the Specification:

Please replace the paragraph that bridges pages 25-26 with the following paragraph. Applicants have omitted the underlining of volume numbers of journal article citations that appeared in the Applicant's original specification as submitted in PCT/EP2003/013021 to avoid any confusion with amendments to the specification. Applicants note that the Office omitted such underlining in paragraph 0089 of US 2006/0075524 A1, the US patent application publication of the instant application.

Intein-mediated trans-splicing of proteins with restoration of their activity is known in the prior art and is described in detail in many publications. Protein affinity interaction and/or trans-splicing can be achieved by using engineered inteins. Inteins were first identified as protein sequences embedded in-frame within protein precursor and excised during the protein maturation process (Perler et al., 1994, *Nucleic Acids Res.*, 22, 1125-1127; Perler, F. B., 1998, *Cell*, 92, 1-4). All information and catalytic groups necessary to perform a self-splicing reaction reside in the intein and two flanking amino acids. The chemical mechanism of protein splicing is described in detail by Perler and colleagues (1997, *Curr. Opin. Chem. Biol.*, 1, 292-299) and by Shao & Kent (1997, *Chem. Biol.*, 4, 187-194). Inteins usually consist of N- and C-terminal splicing regions and a central homing endonuclease region or small linker region. Over 100 inteins are known so far that are distributed among the nuclear and organellar genomes of different organisms including eukaryotes, archaeobacteria and eubacteria (<http://www.neb.com/neb/inteins.html>). It was shown that inteins are capable of trans-splicing. The removal of the central homing endonuclease region does not have any effect on intein self-splicing. This made possible the design of trans-splicing systems, in which the N-terminal and C-

terminal fragments of an intein are co-expressed as separate fragments and, when fused to exteins (protein fragments that are ligated together with the help of the Intein), can perform trans-splicing in vivo (Shingledecker et al., 1998, *Gene*, 207, 187-195). It was also demonstrated with N- and C-terminal segments of the *Mycobacterium tuberculosis* RecA intein, that protein trans-splicing can take place in vitro (Mills et al., 1998, *Proc. Natl. Acad. Sci. USA*, 95, 3543-3548). This phenomenon was also identified for DnaE protein of *Synechocystis* sp. strain PCC6803 (Wu et al, 1998, *Proc. Natl. Acad. Sci. USA*, 95, 9226-9231). Two different genes located more than 700 Kb.p. apart on opposite DNA strands encode this protein. It was also shown that two intein sequences encoded by those genes reconstitute a split mini-intein and are able to mediate protein trans-splicing activity when tested in *Escherichia coli* cells. An intein of the same origin (DnaE intein from *Synechocystis* sp. strain PCC6803) was used to produce functional herbicide-resistant acetolactate synthase II from two unlinked fragments (Sun et al., 2001, *Appl. Environ. Microbiol.*, 67, 1025-29) and 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS) (Chen et al., 2001, *Gene*, 263, 39-48) in *E. coli*.